

# THE ROLE OF INTRAOPERATIVE ULTRASONOGRAPHY IN PANCREATIC SOLID TUMOR STAGING

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Significant advances in preoperative diagnostic techniques have slightly reduced the value of intraoperative ultrasonography (IOUS, sonography) for pancreatic tumor diagnosis. However, tumor extension degree is finally determined during intraoperative revision. IOUS is a technique, which enables to assess a tumor process extension degree and perform minimally invasive surgeries for morphological verification of the changes revealed.

**The aim of the investigation** was to assess the capabilities of intraoperative ultrasound investigation to determine the degree of pancreatic tumor extension.

**Materials and Methods.** 53 patients with morphologically verified diagnosis of pancreatic tumor underwent IOUS. We assessed if the tumor extended beyond the pancreatic capsule involving the surrounding cellular tissue, magistral vessels, and revealed metastases in lymph nodes and liver. If there were N<sub>3</sub> (according to JPS, Japan Pancreatic Society) metastases in lymph nodes or in liver, they were needed.

**Results.** 10 patients underwent test laparotomy following IOUS. Laparotomy resulted from: the involvement of the superior mesenteric vein up to the inflows (4 patients), liver metastases (2 patients), peritoneal dissemination (3 patients), liver metastases and peritoneal dissemination (1 patient). IOUS accuracy in determining the tumor extension beyond the pancreatic capsule was 98%. We distinguished two types of surrounding cellular tissue infiltrated by the tumor: focal and diffuse. IOUS sensitivity, specificity and accuracy in vascular invasion determination were 96, 93.3 and 95% respectively. Lymph gland metastases (N<sub>3</sub> according to JPS) were detected in 5 patients; the lymph nodes being needed for morphological verification of tumor changes. Liver metastases were found in 3 patients. Paracentesis was performed for morphological verification of a tumor.

**Conclusion.** Intraoperative ultrasonography is a highly informative diagnostic technique used to determine the degree of pancreatic tumor extension. Moreover, IOUS enables to perform morphological verification to detect distant metastases (primarily, in liver and distant lymph nodes) with low complication rate.

**Key words:** pancreatic tumor; pancreatic carcinoma; intraoperative ultrasonography.

Tumors of the pancreas are presented by a heterogeneous group of neoplasms diverse in their histological structure. Duct adenocarcinoma (cancer of the pancreatic gland — CPG) [1] makes the majority of the tumors (85–90%). Statistical data testify to the steady growth of CPG morbidity in the developed countries for the last decades. According to the world statistics most of the CPG cases (up to 80%) are revealed in the locally spread process or in the presence of distant metastases. In Russia 13208 new cases of malignant pancreatic oncopathology were found during 2012: the IV stage was diagnosed in 60.3 % of the patients, the III stage — in 21.2%, I and II — only in 2.2 and 10.2%, respectively; in 6.1% of new registered cases the stage of CPG was not established [2]. CPG stands fourth by the incidence rate among the malignant neoplasms of the gastrointestinal tract in Russia, and first — by the lethality rate. Significantly less frequent neuroendocrine

tumors (1–2% cases of all pancreatic tumors), nonorgan tumors (schwannomas, hemangiomas, less than 1% of cases), tumors of the lymphatic system (non-Hodgkin's lymphomas, less than 1% of cases), metastatic tumors (metastases from cancers of the lung, stomach, large intestine, kidney, ovary — 1.9–2% cases) [3] are found in the pancreas.

The only radical method of treating pancreatic tumors is a surgical one. It may be an independent surgical operation or a stage in the complex therapy.

In the last decades methods of preoperative diagnosis of the pancreatic tumors are being actively developed, enabling to obtain detailed information on the extension of the oncologic process. However, the final decision in determining the extent of the surgical intervention depends on the data of the intraoperative revision. This revision of the surgical operation extent may be connected with the considerable local extension of the tumor, revealing

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of the signs of implantation metastasizing (peritoneal dissemination), metastases to the liver, assessment of the vascular invasion degree. The share of the trial laparotomies in potentially resectable tumors remains sufficiently high. On the other hand, S.V. Shrikhande et al. [4] showed, that a conventional (border-line) resectability of the oncologic process, determined at the preoperative stage, is not always true. Their study included 12 patients with pancreatic tumors and the signs of great vessel involvement. In 5 patients in the course of intraoperative revision the tumor was qualified to be resectable, no signs of the vascular invasion were revealed, and surgical intervention in the extent of R<sub>0</sub> was performed.

**The aim of the investigation** was to assess the capabilities of intraoperative ultrasound investigation in determining the degree of pancreatic tumor extension.

**Materials and Methods.** 53 patients (13 males and 40 women), undergoing treatment for the tumors of the pancreas at the Department of the Abdominal Oncology of Moscow Research Oncological Institute named after P.A. Gertsen in the period from 2011 to 2013, were included into the study. The age of the patients ranged from 18 to 78 years (the average age — 60.60±6.98 years). In 41 patients the tumor was located in the pancreas head, in 12 it was in the body and the tail. All patients underwent abdominal US, computed tomography of the abdominal and chest organs, pancreas tumor biopsy.

The study was conducted according to the Declaration of Helsinki (the Declaration was passed in Helsinki, Finland June, 1964 and revised in October, 2000 (Edinburgh, Scotland), and was performed following approval by the ethic committee of MROI named after P.A. Gertsen. Written consent was obtained from every patient.

During intraoperative revision intraoperative ultra-

sound study (IOUS) using the apparatus VIAMO (Toshiba, Japan) was carried out according to the following scheme:

1) determination of extension of the tumor beyond the gland capsule, assessment of the degree of the adjacent cellular tissue infiltration;

2) determination of the degree of tumor invasion into the great vessels;

3) revealing tumor-altered lymphatic nodes in the zones of distant metastasizing (mesocolon, mesentery, paraaortic regions);

4) IOUS of the liver;

5) IOUS-guided paracentesis of the focal formations in the liver, and the revealed tumor-altered lymphatic nodes of distant metastasizing zones.

The extent of the surgical intervention is shown in Table 1.

In 12 patients a trial surgical intervention was performed. Reasons for explorative laparotomy were: involvement of the superior mesenteric vein in the tumor up to the inflows in 4 patients, metastases to the liver — in 4; dissemination over the peritoneum — in 3; metastases to the liver and dissemination over the peritoneum — in 1.

**Results.** During intraoperative revision IOUS was performed to all patients. The data obtained allowed to determine the degree of local tumor extension and reveal metastases in the liver and distant lymphatic nodes, to make paracentesis of the changes revealed.

**Determination of the pancreatic tumor type.**

Tumors of the pancreas were confirmed in all the patients. We assessed the following echographic characteristics in the mode of the grey-scale echography: localization, size, homogeneity (homogeneous, heterogenous), structure (solid, solid-cystic), echogenicity, (hypogenic, isoechogetic, hypergenic formations), smoothness and clearness of the contour. In the mode of coloured

Table 1

**The extent of the performed surgical management**

Type of the operation	Number of the patients (n=53)		
	Total	R <sub>0</sub>	R <sub>1</sub>
Gastropancreatoduodenal resection	5	3	2
Gastropancreatoduodenal resection + resection of the portal vein and superior mesenteric vein	1	1	0
Pylorus-saving pancreatoduodenal resection	18	15	3
Pylorus-saving pancreatoduodenal resection + resection of the portal vein	1	1	0
Pylorus-saving pancreatoduodenal resection + resection and prosthetic repair of the portal vein	1	1	0
Pylorus-saving pancreatoduodenal resection + resection of the superior mesenteric vein	2	2	0
Distal resection of the pancreas	6	6	0
Coprocaudal resection of the pancreas	2	2	0
Operation Appleby	2	2	0
Pancreatectomy	1		1
Pancreatectomy resection + resection and prosthetic repair of the portal vein	1	1	0
Subtotal resection of the pancreas	1	1	0
Explorative laparotomy	12	—	—

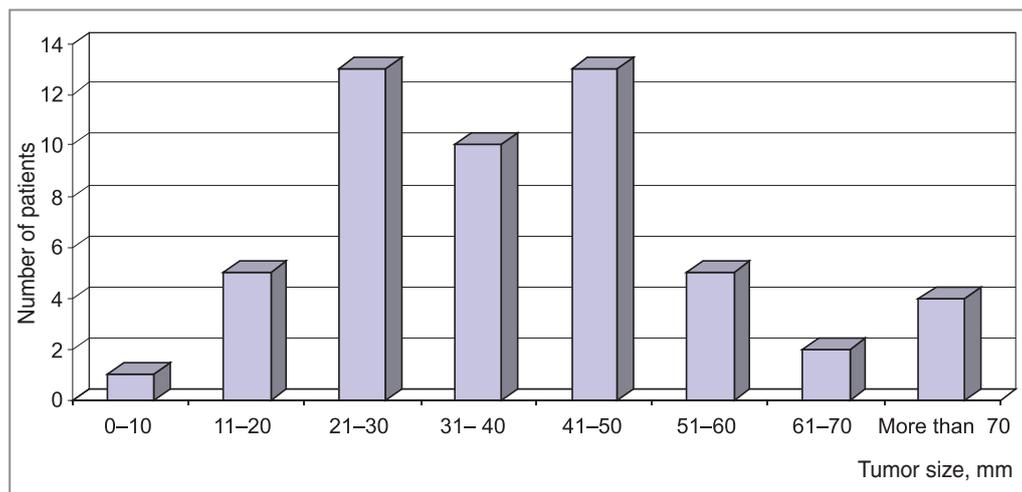


Fig. 1. Distribution of patients according to the pancreas tumor size

Doppler mapping tumor vascularization was evaluated (absence of vascularization, single vessels in the tumor depth, increased vascularization).

The tumor was localized in the pancreas head in 38 patients, in the body — in 5, in the tail — in 8. The mean size of the tumor amounted to 38.5 mm, the least one was 10 mm, and the greatest — 120 mm (Fig. 1). The preoperative diagnostic paracentesis revealed pancreatic adenocarcinoma in 46 patients, neuroendocrine tumor of the pancreas — in 7.

Table 2  
Distribution of the pancreas tumors according to echographic criteria

Sign	Adeno-carcinoma	Neuroendocrine tumor
1. Formation echogenicity (relative to PG tissue)		
Decreased	42	6
Not changed	2	—
Increased	—	—
Mixed	2	1
2. Formation homogeneity		
Homogeneous	1	—
Heterogeneous	45	7
3. Formation structure		
Solid	43	2
Solid-cystic	3	5
4. Formation contour		
Clear	1	5
Unclear	45	2
Smooth	2	5
Irregular	44	2
5. Formation vascularization		
Vascularization absence	43	—
Single vessels in the tumor depth	3	3
Increased vascularization	—	4

Echographic signs of the pancreatic tumors were distributed in the way shown in Table 2.

Adenocarcinomas had hypoechogenic (91.3%), isoechogenic (4.35%) or mixed echogenicity (4.35%). The structure of the most cases was heterogeneous (97.8%) and solid (93.5%), much rarer it was homogeneous (2.2%) and solid-cystic (6.5%). The contour of adenocarcinomas was mainly unclear (97.8%), irregular (95.7%). In the depth of adenocarcinomas single vessels were detected only in 3 patients, in the rest cases (93.5%) the blood flow was not determined in the mode of color Doppler mapping.

Neuroendocrine tumors (NET) had mainly decreased (85.7%) echogenicity and solid-cystic structure (71.4%), less commonly mixed echogenicity (14.3%) and solid structure (28.6%). NET contour in the majority of cases was smooth and clear (71.4%). In the mode of coloured Doppler mapping an intensive blood flow was determined in 57.1% of cases, or single vessels in the tumor depth in 42.9% of cases.

**Determining the degree of pancreatic tumor extension.** The degree of extension of the tumor changes in the pancreatic gland was evaluated on the basis of the following facts: extension of the tumor beyond the gland “capsule”, involvement of the surrounding cellular tissue in the tumor, involvement of adjacent organs. Criterion of extension of the tumor beyond the gland “capsule” was bulging out the tumor beyond the contour of the pancreas. IOUS found out 7 localized pancreatic tumors: CPG (15 mm and 20 mm tumor size), and 5 neuroendocrine tumors (the greatest size — 50 mm). In one patient with CPG initial invasion of retropancreatic cellular tissue, not detected by IOUS, was revealed by means of the planned morphological investigations. The accuracy of IOUS in determining tumor extension beyond the pancreas capsule was 98.1%.

Localized tumor of the pancreas head is presented on Fig. 2. The tumor has a mixed echogenicity, heterogeneous

structure, smooth, unclear contour. It is localized in the depth of the gland parenchyma.

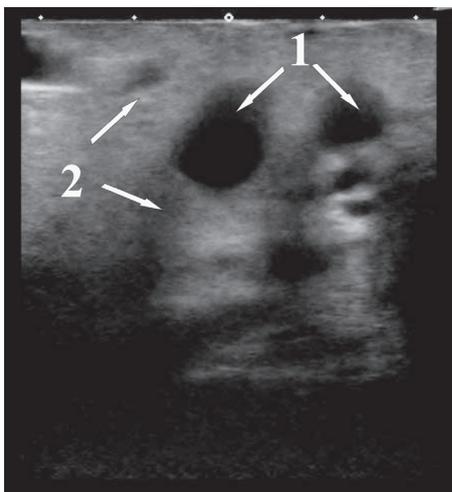
Retropancreatic cellular tissue (along the posterior surface of the pancreas), the tissue around the celiac trunk, around the superior mesenteric artery (at the site of its diversion from the aorta), paranephral cellular tissue, tissue of the root of mesentery were referred by us to the surrounding cellular tissue.

Considering the data of involvement of the cellular tissue in the tumor, two types of infiltration of the surrounding tissue by the tumor were distinguished: focal and diffuse. In the focal type the tumor changes spread into the surrounding cellular tissue, have smooth or irregular, clear contour, and echographic structure similar to the tumor. In the focal type retropancreatic tissue is infiltrated — in 46 patients, the tissue around the celiac trunk — in 2 patients, cellular tissue around the superior mesenteric artery and of the root of the mesentery — in 2 patients.

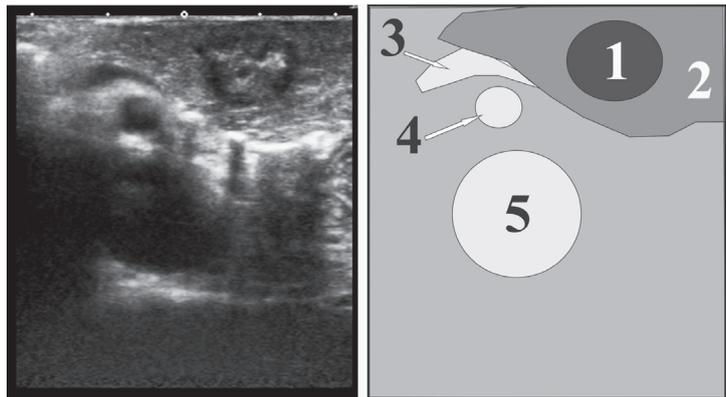
In diffuse type the contour of the tumor is not visualized, as well as the boundary line of the tumor and surrounding cellular tissue. The cellular tissue is diffusely thickened like “edema”. In the diffuse type retropancreatic cellular tissue is infiltrated — in 3 patients, the cellular tissue of the thin bowel mesentery root — in 2, and paranephral tissue — in 1 patient.

Fig. 3 shows the tumor of the pancreas body with the focal infiltration of the retropancreatic cellular tissue. The tumor has a decreased echogenicity, heterogeneous structure, and a clear irregular contour. The focal infiltration of the retropancreatic cellular tissue has an echo-structure similar to that of the tumor, its contour is clear and irregular.

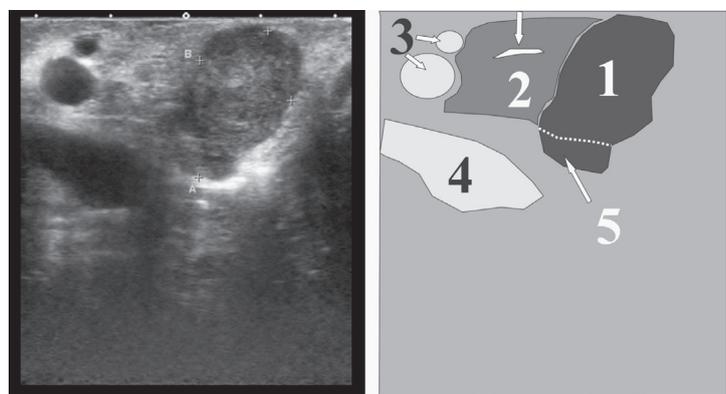
Diffuse tumor infiltration of the root of the thin bowel



**Fig. 4.** Diffuse tumor infiltration of the cellular tissue of the thin bowel mesentery root: 1 — superior mesenteric artery and vein; 2 — diffuse tumor infiltration of the mesentery root tissue



**Fig. 2.** Localized tumor of the pancreas body: 1 — tumor; 2 — unchanged tissue of the pancreas; 3 — splenic vein; 4 — superior mesenteric artery; 5 — aorta



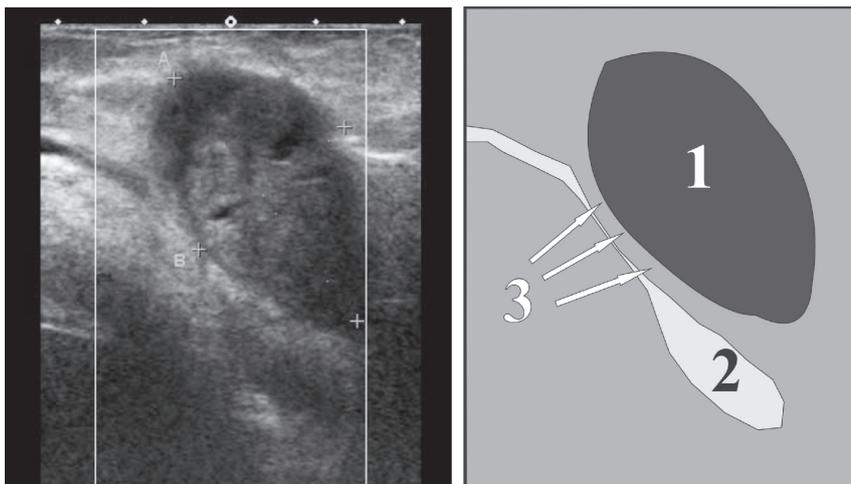
**Fig. 3.** Focal tumor infiltration of the retropancreatic tissue: 1 — tumor of the pancreas body; 2 — unchanged pancreatic tissue (Wirsung's duct is marked by a white arrow); 3 — artery and vein of the spleen; 4 — left kidney artery; 5 — focal tumor infiltration of the retropancreatic cellular tissue

mesentery is presented on Fig. 4. The cellular tissue is consolidated and infiltrated. The vessel wall contour is smooth, unclear.

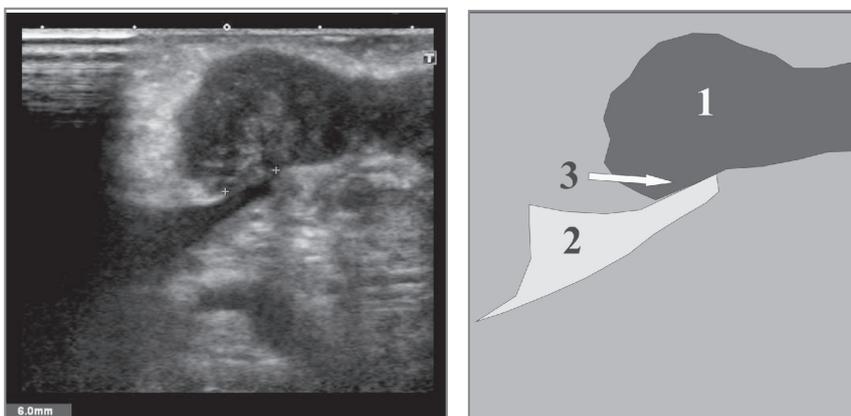
**Determining the vascular invasion by the pancreatic tumor.** The criteria of the involvement of the vein wall in the tumor were: extension of the contact between the tumor and venous wall over 10 mm, adjunction of the tumor exceeding 90° of the vessel cross-section, absence of the hyperechogenic layer between the vessel and the tumor (Fig. 5–7). Sensitivity, specificity, and accuracy were equal to 96, 93.3 and 95%, respectively.

Criteria of the involvement of the artery wall were: extension of the vessel and tumor contact over 10 mm, adjunction exceeding 90° of the vessel cross-section, absence of the hyperechogenic layer between the vessel and the tumor, irregular vessel contour, vessel stenosis.

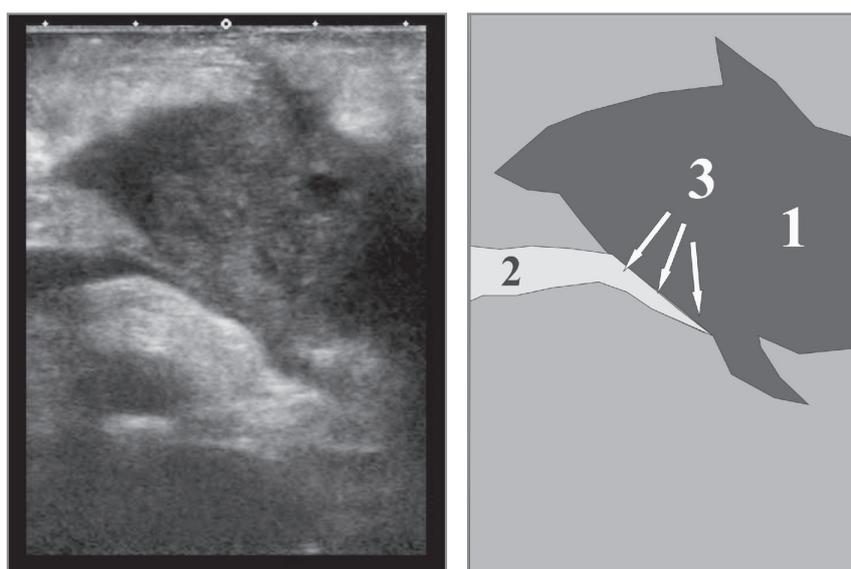
In our investigation 2 patients were determined to have involvement of the celiac trunk by the tumor, and 8 patients — of the spleen artery. In one patient involvement of the celiac trunk and spleen artery was false-positive



**Fig. 5.** Tumor of the pancreas body, compressing but not involving the wall of the vein: 1 — tumor; 2 — splenic vein; 3 — hyperechogenic tissue between the tumor and the compressed vessel wall



**Fig. 6.** Local ingrowth of the pancreas body to the wall of the vein: 1 — tumor; 2 — splenic vein; 3 — a region of tumor ingrowth to the vein wall



**Fig. 7.** Ingrowth of the pancreas body to the wall of the vein: 1 — tumor; 2 — splenic vein; 3 — ingrowth of the tumor to the vein wall

according to the results of the planned pathomorphological study together with the events of curative pathomorphosis of the IV degree after neoadjuvant chemotherapy. In the remaining patients the artery wall involvement was confirmed by the findings of the planned morphological study.

**Determining metastatic lesions of the lymphatic nodes.** Performing IOUS of the distant metastasizing zones (paraaortic areas, lesser omentum, mesentery of the small and large intestine) changed lymphatic nodes of the small intestine mesentery were found in 2 patients, gastrocolic ligament — in 1 patient, and paraaortic areas — in 2 patients. The criteria of metastatic node lesions were: the cross-section dimension over 10 mm, hypoechogenic structure, absence of cortico-medullar differentiation, unclear, irregular contour. US-controlled paracentesis confirmed cytologically metastases of adenogenic cancer.

**Determining metastases to the liver.** Focal formations in the liver were found in 5 patients. In 4 patients intraoperative revision revealed metastases 15, 13, 16 and 11 mm in size (Table 3).

US examination failed to reveal any formations in the liver in 1 patient, in 4 patients they were determined. Some difficulty of preoperative diagnosis arose due to the similar echographic image of the metastases and liver hemangioma (patient 1), metastases and reactive inflammation (patients 2 and 3), and metastases and zone of local liver fibrosis (patient 5). Comparing the echographic characteristics it was noted, that during IOUS metastases had the echostructure different from the US data. Echogenicity of metastases during IOUS was mainly mixed (60%), the structure in all formations was heterogeneous, solid, the contour was irregular and unclear (Fig. 8). In the majority of metastases in the course of IOUS in the mode of color Doppler mapping a blood flow was determined in the depth of the formation.

Table 3

## Characteristics of the patients with focal liver formations

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Possibility of visualization	Yes	Yes	Yes	No	Yes
Formation size, mm	15	13	11	—	16
Echogenicity	Increased	Increased	Slightly increased	—	Increased
Formation contour (smooth, irregular, clear, unclear)	Clear, irregular	Clear, smooth	Unclear, smooth	—	Clear, irregular
Vascularization	Single vessels in the depth of the formation	Single vessels in the depth of the formation	Absence of vascularization	—	Absence of vascularization
Formation biopsy	No	Yes	Yes	—	No
Results	—	Reactive inflammation	Reactive inflammation	—	—
IOUS	Formation of mixed echogenicity with clear irregular contour, up to 15 mm in size	Formation of increased echogenicity, with clear irregular contour, up to 13 mm in size	Formation of increased echogenicity, with unclear smooth contour, up to 11 mm in size	Formation of slightly decreased echogenicity with unclear irregular contour, up to 13 mm in size	Formation of mixed echogenicity with unclear contour, up to 16 mm in size
Results of the repeated biopsy	Adenocarcinoma	Adenocarcinoma	Reactive inflammation	Adenocarcinoma	Adenocarcinoma

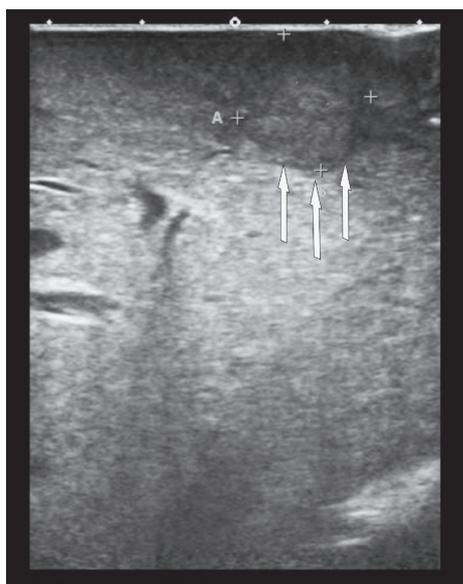


Fig. 8. Subcapsular liver metastasis (marked by the white arrows)

**Diagnostic minimally invasive interventions.** If, at the stage of intraoperative revision, metastases to the distal lymphatic nodes and to the liver were suspected, inspiration paracentesis of the revealed changes was performed, obtaining sufficient material for cytological investigation. In all cases tumor character of the changes was confirmed: in 5 patients — by the puncture of the lymphatic nodes, in 4 patients — by the liver puncture.

**Discussion.** IOUS method has been used from the end of 80-s of the XX century [5–9]. Recently, the

value of this method slightly decreased due to the active development of the preoperative diagnostic methods (computed tomography, magnetic resonance tomography, endoscopic ultrasonography, positron emission tomography). However, final decision on the necessity of tumor resection is made at the stage of intraoperative revision. Application of IOUS allows to obtain full information on the extension of the oncological process.

Numerous investigations underline a high sensitivity of the method in revealing initial and metastatic tumors of the abdominal cavity and retroperitoneal region, which varies from 93 to 100% [10–13]. Resectability of the pancreatic tumor depends on the interrelations between the tumor and surrounding vessels. IOUS makes it possible to determine the invasion of the vessels by the tumor with a high accuracy. In the studies by M. Sugiyama et al. [13] the sensitivity of sonography in evaluation of vascular invasion amounted to 93%. Sensitivity, specificity and accuracy of sonography in evaluation of venous invasion according to the data of our investigation were 96, 93.3 and 95%, respectively.

The extension of the tumor to the adjacent cellular regions may be a factor which makes the resectability doubtful. In the given work two types of tumor infiltration were distinguished: focal and diffuse. Diffuse type of tumor infiltration was confirmed by the findings of cytological examination, and was accompanied by numerous metastases to the lymphatic nodes in comparison with other cases.

Revealing metastases of liver damage by means of IOUS enables to revise the tactics of patient

management, not to use the radical surgical treatment, or to change the extent of surgical intervention (as a rule, in neuroendocrine pancreatic tumors). The sensitivity of IOUS in revealing liver metastases reaches 95% [13]. In this investigation the authors compared echoimages of the revealed liver lesions using transabdominal US and IOUS and determined, that such echographic parameters as echogenicity, heterogeneity, clearness and smoothness of the liver lesions in these methods may be different.

**Conclusion.** Intraoperational ultrasound examination is a highly informative method of diagnosis and determination of the pancreatic tumor extension. The possibility of morphological verification in determining distal metastases (firstly to the liver and distant lymphatic nodes) with a low risk of complications is an important adjunct of IOUS.

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